REMARKS

Applicant respectfully requests reconsideration. Claims 1, 4-9, 12, 13, 15-20, 22, 25-28, 129, 135-142 and 144-146 were previously pending in this application. Claim 136 has been amended. Applicant reserves the right to pursue the subject matter of originally filed claims in one or more continuation applications. No new matter has been added.

Claims 1, 4-9, 12, 13, 15-20, 22, 25-28, 129, 135-142 and 144-146 are pending for examination with claims 1, 136, 137, 138, 139 and 141 being independent claims.

Rejection under 35 U.S.C. §112

Claim 136 is rejected under 35 U.S.C. §112, first paragraph, enablement.

Applicant has amended claim 136 to recite that the oligonucleotide, the antigen, and the non-oligonucleotide mucosal adjuvant are all administered by the same route.

Reconsideration and withdrawal of this rejection is respectfully requested.

Rejection under 35 U.S.C. §103

Claims 1, 4-9, 12, 13, 15-20, 22, 26-28, 129, 135-142 and 144-146 are rejected under 35 U.S.C. §103(a) as being unpatentable over Krieg et al. (US 6,239,116) in view of Hutcherson et al. (US 6,727,230) or Agrawal et al. (US 6,426,334) and evidenced by McCluskie et al. (*Vaccine* 19:413-422, 2001).

Applicant has previously rebutted the rejection on the basis that a prima facie case of obviousness has not been made by the Examiner at least because one of ordinary skill in the art would not have been motivated to combine the references as suggested by the Examiner and the combination of references does not result in each and every limitation of the rejected claims.

One of ordinary skill in the art would not have been motivated to combine Krieg et al. with Hutcherson et al. as suggested by the Examiner. The Examiner's rationale is based on a misstatement. The Examiner considers that Hutcherson et al. teaches that its oligonucleotides have unmethylated CG dinucleotides that impart immunostimulatory activity. Applicant disagrees. When read as a whole, Hutcherson et al. teaches oligonucleotides that are immunostimulatory

because they have at least one phosphorothioate internucleotide bond. Hutcherson et al. does not teach that such oligonucleotides must contain an unmethylated CG dinucleotide in order to be immunostimulatory.

The Examiner's basis for combining Krieg et al. with Hutcherson et al. is that both references teach the same class of immunostimulatory oligonucleotides. This is incorrect and cannot form the basis of the motivation to combine the references.

To be sure, Krieg et al. teaches oligonucleotides that are immunostimulatory in a sequence-dependent manner, while Hutcherson et al. teaches oligonucleotides that are immunostimulatory in a sequence-independent manner. One of ordinary skill in the art would not have substituted the sequence-dependent oligonucleotides of Krieg et al. in the methods of Hutcherson et al. which teach the use of sequence-independent oligonucleotides, and any suggestion to the contrary is based on hindsight.

Similarly, one of ordinary skill in the art would not have been motivated to combine Krieg et al. with Agrawal et al., as suggested by the Examiner. Agrawal et al. teaches administration of a CG oligonucleotide to a subject to induce IL-12 levels and thus produce a therapeutic result. Agrawal et al. does not describe the combination of a CG oligonucleotide with an antigen to produce an antigen specific immune response. The Examiner has suggested that the teachings of Krieg et al. with respect to producing an antigen specific immune response by co-administering an antigen and a CG oligonucleotide can simply be substituted into the teachings of Agrawal of inducing an IL-12 immune response. It is unclear why one of skill in the art would make such a substitution in the absence of hindsight reasoning.

The Examiner further states as a basis for motivation to combine the references that "these specific routes of delivery (i.e., intranasally, rectally, vaginally, orally and inhalation) have been routinely and successfully used for delivering for (sic) a synthetic oligonucleotide containing an unmethylated CpG motif to induce an immune response in an infectious subject or a tumor bearing subject as taught by either Hutcherson et al. or Agrawal et al." Applicant notes that the working examples of both references employ non-mucosal routes.

Finally neither combination suggested by the Examiner results in every limitation of the rejected claims. Each of the rejected claims requires administration to a subject in need of a

mucosal immune response. None of the cited references teaches treatment of subjects in need of a mucosal immune response. None of the references even teaches that mucosal routes of administration are preferable over non-mucosal routes. For example, the working examples of Hutcherson et al. all employ intradermal administration and those of Agrawal et al. employ either intraperitoneal or subcutaneous administration. These are not mucosal administration routes, and there is no evidence that they induce a mucosal immune response and that the subjects to whom the oligonucleotides were administered were in need of such a response.

As taught in the specification, a mucosal immune response is characterized by the presence of sIgA in mucosal tissues. This immune response is not a systemic immune response. Agrawal et al. teach a method for inducing systemic IL-12 levels. The Examiner has not provided any evidence that the IL-12 immune response taught by Agrawal et al. is a mucosal immune response.

The Examiner equates subjects having an immune system deficiency such as cancer or an infection with subjects in need of a mucosal immune response. This statement is unsupported and more importantly incorrect. Applicant requested the Examiner to support that statement with evidence. The Examiner has not done so and instead continues to rely on this unsupported statement. McCluskie et al. does not provide this teaching either.

Reconsideration and withdrawal of this rejection is respectfully requested.

Claim 25 is rejected under 35 U.S.C. §103(a) as being unpatentable over Krieg et al. (US 6,239,116) in view of Hutcherson et al. (US 6,727,230) or Agrawal et al. (US 6,426,334) and evidenced by McCluskie et al. (Vaccine, 19: 413-422, 2001) and in further view of Craig et al. (US 6,689,757).

Applicant respectfully traverses. The combination of Krieg et al. with either Hutcherson et al. or Agrawal et al., as evidenced by McCluskie et al., does not render obvious claim 1 for the reasons stated above. Claim 25 depends from claim 1. Craig et al. does not cure the deficiencies in the combination of references.

Moreover, Craig et al. requires dual delivery of an epitope (or antigen) in its peptide or polypeptide form and a nucleic acid encoded epitope (or antigen). Claims 1, 136-139 and 144 all explicitly recite that the antigen is not encoded in a nucleic acid vector. Applicant presented this

argument in its last response, however the Examiner failed to consider it. See page 18, first three paragraphs. The Examiner has provided no response as to how the combination of Krieg et al. with either Hutcherson et al. or Agrawal et al. (as evidenced by McCluskie et al.) taken together with Craig et al. creates a prima facie case of obviousness when the combination does not render each and every limitation of the rejected claim. Specifically, claim 25 requires administration of an antigen, provided the antigen is not encoded in a nucleic acid vector. The method of Craig et al. requires administration of an epitope (or antigen) in the form of the nucleic acid that encodes it. The combination of these references therefore yields a method that requires administration of nucleic acid that encodes an epitope (or antigen). Claim 25 specifically excludes such a limitation. Accordingly, the combination does not yield each and every limitation of the claim, and a prima facie case has not been made.

Reconsideration and withdrawal of this rejection is respectfully requested.

Claims 136 and 142 are rejected under 35 U.S.C. §103(a) as being unpatentable over Briles et al. (US 6,042,838) in view of Krieg et al. (US 6,194,388) and evidenced by McCluskie et al. (Vaccine, 19:413-422, 2001).

Claim 136 has been amended to recite that the oligonucleotide, the non-oligonucleotide mucosal adjuvant, and the antigen are all administered rectally, vaginally or ocularly. Briles et al. teaches administration of PSPA to olfactory mucosa (via intranasal administration), respiratory mucosa, gingival mucosa, and alveolar mucosa, in order to prevent or treat colonization of Streptococcus pneumoniae. Neither Briles et al. nor Krieg et al. teach administration of antigen and/or adjuvant (such as CG oligonucleotides) rectally, vaginally or ocularly, and thus the combination does not yield each and every limitation of the rejected claims. Moreover, one of ordinary skill in the art would not be motivated to administer the PSPA of Briles et al. rectally, vaginally or ocularly since Briles et al. teaches that Streptococcus pneumoniae colonize the upper airways and are maintained in the nasopharynx. Krieg et al. does not provide this motivation either. As a result, not only is there no motivation for modifying the teachings in this way, there is also no reasonable expectation of success of preventing or treating Streptococcus pneumoniae infection by administering antigen and adjuvant rectally, vaginally or ocularly.

For at least these reasons, a prima facie case of obviousness has not been made. Reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Dated: January 30, 2008

Respectfully submitted,

By _____

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